REMARKS

Claims 71-99 have been canceled. New claims 100-128 are based on claims 71-99 and are pending in the present application.

It is respectfully submitted that the present amendment presents no new issues or new matter and places this case in condition for allowance. Reconsideration of the application in view of the above amendments and the following remarks is requested.

I. Information Disclosure Statement

The Office Action indicated that since the IDS submitted during the prosecution of U.S. Patent No. 6,146,869 was not made of record by the Examiner in that case, Applicants are advised that should they desire that other references be considered, a new IDS must be filed that meets the requirements of 37 CFR 1.97 and 1.98. Applicants submit a new IDS that meets the requirements of 37 CFR 1.97 and 1.98, including the proper fee.

II. The Rejection of Claim 78 under 35 U.S.C. § 112, First Paragraph

Claim 78 stands rejected under 35 U.S.C. § 112, first paragraph, as "as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." Specifically, the Office Action states the "specification as originally filed does not disclose this fragment of SEQ ID NO:2, nor that this fragment has phospholipase activity. ... It appears that recitation of '264' is a typographical error; and should be –464--."

In response, Applicants confirm that a typographical error was made in claim 78 and have corrected the error in new claim 107 to read "464."

For the foregoing reason, Applicants submit that the new claim overcomes the rejection under 35 U.S.C. § 112 and respectfully request reconsideration and withdrawal of the rejection.

III. The Rejection of Claims 71-75, 79-82, 84-87, and 91-95 under 35 U.S.C. § 112, First Paragraph

Claims 71-75, 79-82, 84-87, and 91-95 stand rejected under 35 U.S.C. § 112, first paragraph, "as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." Specifically, the Office Action states:

> Claims 71-75, 79-82, 84-87, and 91-95 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid sequence encoding phospholipase B wherein either the nucleic acid sequence comprises nucleotides 568 to 2045 of SEQ ID NO:1 or the polypeptide comprises amino acids 20-464 of SEQ ID NO:2, does not reasonably provide enablement for any other embodiments lying outside this scope.

This rejection is respectfully traversed.

The instant invention is directed to isolated nucleic acid sequences encoding a polypeptide having phospholipase B activity, selected from the group consisting of: (a) a nucleic acid sequence encoding a polypeptide having an amino acid sequence which has at least 80% identity with amino acids 20 to 464 of SEQ ID NO:2; (b) a nucleic acid sequence having at least 80% homology with nucleotides 568 to 2045 of SEQ ID NO:1; (c) a nucleic acid sequence which hybridizes under medium stringency conditions with (i) nucleotides 568 to 2045 of SEQ ID NO:1, (ii) the cDNA sequence contained in nucleotides 568 to 2045 of SEQ ID NO:1, or (iii) a complementary strand of (i) or (ii); and (d) a subsequence of (a), (b), or (c), wherein the subsequence encodes a polypeptide fragment which has phospholipase B activity.

Applicants have shown that the closest protein with any homology to the instant phospholipase B is a phospholipase C, not a phospholipase B. The comparative alignment showed that the *Aspergillus oryzae* HowB430 phospholipase B shares 26% identity with a phospholipase C from *Pseudomonas aeruginosa* (SwissProt Acc. No. P15713). Applicants have, therefore, discovered a new class of phospholipase B, with only a very distant relationship to known phospholipases C, but no relationship to known phospholipases B. The Office Action supports Applicants' position by stating: "A search of the protein databases by the PTO failed to reveal that any prior art phospholipase B ... shares significant homology with the instant phospholipase B." However, the Office Action asserts that the claims should be limited to the nucleic acid sequence of SEQ ID NO:1 or the amino acid sequence of SEQ ID NO:2.

Claims limited to the nucleic acid sequence of SEQ ID NO:1 or the amino acid sequence of SEQ ID NO:2 would not adequately protect the inventors. One of ordinary skill in the art could make, for example, one or more conservative amino acid changes in the sequence of SEQ ID NO:2. Such conservative substitutions are, for example, within the group of basic amino acids (arginine, lysine and histidine), acidic amino acids (glutamic acid and aspartic acid), polar amino acids (glutamine and asparagine), hydrophobic amino acids (leucine, isoleucine and valine), aromatic amino acids (phenylalanine, tryptophan and tyrosine), and small amino acids (glycine, alanine, serine, threonine and methionine). Moreover, other changes in SEQ ID NO:2 of a minor nature could also be made,

naturally or recombinantly, that do not change the inherent properties of the phospholipase B of SEQ ID NO:2. Thus, based on the teachings of the present application, one skilled in the art could find another phospholipase B having essentially the same properties of the phospholipase B of the instant invention and thereby circumvent the literal scope of Applicants' patent rights.

The Office Action states that "[a]ll the specification does is provide a possible plan for obtaining other nucleic acid sequences embraced by the claims, the success of which is completely unclear." Applicants respectfully disagree. As the September 14, 2001 amendment of record demonstrates, Applicants have detailed on page 5, line 1, to page 7, line 7, of the specification, instructions for performing standard Southern hybridization under medium, medium-high, and high stringency conditions to identify such nucleic acids from other strains, whether of the same or different genera or species. Applicants also detail on page 3, line 25, to page 4, line 7, of the specification, instructions for determining the degree of identity between two amino acid sequences by the Clustal method (Thompson *et al.*, 1994, *Nucleic Acids Research* 22: 4673-4680; Thompson *et al.*, 1997, *Nucleic Acids Research* 25: 4876-4882), and on page 12, line 29, to page 13, line 8, of the specification, the degree of homology between two nucleic acid sequences by the Wilbur-Lipman method (Wilbur and Lipman, 1983, *Proceedings of the National Academy of Science USA* 80: 726-730). Applicants further describe the following probes in the specification for use in conducting the hybridization: (i) nucleotides 568 to 2045 of SEQ ID NO:1, (ii) the cDNA sequence contained in nucleotides 568 to 2045 of SEQ ID NO:1, and (iii) a complementary strand of (i) or (ii). These probes consist of the mature coding region of SEQ ID NO:1, which is the most essential part of the entire phospholipase B gene. Use of this portion of the gene enables the identification and isolation of other genes that are closely related or essentially identical to the gene of SEQ ID NO:1 encoding a polypeptide having phospholipase B activity. Once a gene is isolated and its sequence determined, the deduced amino acid sequence can then be compared to that of SEQ ID NO:2 to ascertain whether it falls within the scope of the instant claims. Moreover, using Applicants' specification, production of the phospholipase B can be achieved and enzymatically assayed to show it has phospholipase B activity. All of these methods are highly predictable and do not require undue experimentation. Consequently, Applicants submit that the information disclosed in the specification combined with the knowledge of the art provides sufficient guidance to one of ordinary skill in the art to isolate such nucleic acids from other strains. The written and enabling description as a whole is sufficient to evidence possession of the claimed nucleic acid sequences because the claimed nucleic acid sequences are defined by relation to the structure of the sequence of SEQ ID NO:1 as well as the inherent properties of the polypeptide encoded by the nucleic acid sequences of SEQ ID NO:1. Thus, there is sufficient written and enabling description in the

specification to direct and guide the skilled artisan to practice the claimed invention.

The facts in the present case are similar to those in In re Wands, supra. There, the claimed invention involved methods for the immunoassay of hepatitis B surface antigen (HBsAg) by using high-affinity monoclonal IgM antibodies having specified properties. A hybridoma cell line that secretes IgM antibodies against HBsAg was deposited at a recognized cell depository. The claims, which were not limited to the deposited cell line, were rejected for lack of enablement. The Federal Circuit reversed the rejection as follows:

> When Wands' data is interpreted in a reasonable manner, analysis ... leads to the conclusion that undue experimentation would not be required to practice the invention. Wands' disclosure provides considerable direction and guidance on how to practice their invention and presents working examples. There was a high level of skill in the art at the time when the application was filed, and all of the methods needed to practice the invention were well known.
>
> The nature of monoclonal antibody technology is that it involves screening hybridomas to determine which ones secrete antibody with desired characteristics. Practitioners of this art are prepared to screen negative hybridomas in order to find one that makes the desired antibody. No evidence was presented by either party on how many hybridomas would be viewed by those in the art as requiring undue experimentation to screen. However, it seems unlikely that undue experimentation would be defined in terms of the number of hybridomas that were never screened.

In re Wands, 8 U.S.P.Q.2d at 1406-07.

Applicants also respectfully submit that requiring applicants to limit the claims to SEQ ID NO:1 or SEQ ID NO:2 would be contrary to public policy as set forth in In re Goffe, 191 U.S.P.Q. 429, 431 (C.C.P.A. 1976):

> For all practical purposes, the board would limit appellant to claims involving the specific materials disclosed in the examples, so that a competitor seeking to avoid infringing the claims would merely have to follow the disclosure in the subsequently-issued patent to find a substitute. However, to provide effective incentives, claims must adequately protect inventors. To demand that the first to disclose shall limit his claims to what he has found will work or to materials which meet the guidelines specified for 'preferred' materials in a process such as the one herein involved would not serve the constitutional purpose of promoting progress in the useful arts.

In the instant case, claims limited to SEQ ID NO:1 or SEQ ID NO:2 would not adequately protect the inventors. Based on the teachings of the present application, one skilled in the art could attempt to find another nucleic acid sequence which encodes a phospholipase B substantially similar or essentially identical as claimed herein and thereby attempt to circumvent the literal scope of Applicants' patent rights.

For the foregoing reasons, Applicants submit that the rejections under 35 U.S.C. § 112 have been overcome. Applicants respectfully request reconsideration and withdrawal of the rejections.

IV. The Rejection of Claim 87 under 35 U.S.C. § 112, First Paragraph

Claims 87 stands rejected under 35 U.S.C. § 112, first paragraph, because "this claim fails to meet the enablement requirement since the deposit made under the Budapest treaty does not meet all of the requirements under 37 CFR 1.801-1.809." Specifically, the Office Action requested a declaration that *E. coli* NRRL B-30142 will be readily available upon the issuance of a patent.

As requested, Applicants enclose a Statement under 37 C.F.R. § 1.808 that the strain was deposited under the Budapest Treaty and all restrictions will be removed upon the granting of the U.S. patent. Applicants therefore submit that this rejection has been overcome.

V. The Rejection of Claims 80-82 and 88-90 under 35 U.S.C. § 112, Second Paragraph

Claims 80-82 and 88-90 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite on two grounds.

Ground 1: The Office Action states that claims 80-82 are indefinite because each recite the limitation "nucleotides 568 to 2045 of SEQ ID NO:2" which lack antecedent basis and should be replaced with –SEQ ID NO: 1–. Applicants have made an inadvertent typographical error in these claims and have corrected the error in the new claims to recite "SEQ ID NO:1."

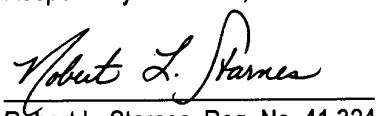
Ground 2: The Office Action states that claims 88-90 are incomplete and confusing because it is unclear how hybridizing a DNA will allow isolation of a nucleic acid sequence, which are different entities. To clarify the meaning of the claim, Applicants have rewritten the claim, now new claim 117, to recite: "An isolated nucleic acid sequence encoding a polypeptide having phospholipase B activity, said nucleic acid sequence obtained by (a) identifying a clone containing a nucleic acid sequence which hybridizes under medium stringency conditions with (i) nucleotides 568 to 2045 of SEQ ID NO. 1, (ii) the cDNA sequence contained in nucleotides 568 to 2045 of SEQ ID NO. 1, or (iii) a complementary strand of (i) or (ii); and (b) isolating the nucleic acid sequence encoding a polypeptide having phospholipase B activity from the clone." The dependent claims have also been rewritten accordingly.

For the foregoing reasons, Applicants submit that the new claims overcome the rejections under 35 U.S.C. § 112. Applicants respectfully request reconsideration and withdrawal of the rejections.

VI. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,



Date: June 7, 2002

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